

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference 900	FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/IL2004/001018	International filing date (day/month/year) 08.11.2004	Priority date (day/month/year) 13.11.2003	
International Patent Classification (IPC) or national classification and IPC C12N5/06, C07K14/715, A61K35/00			
Applicant YEDA RESEARCH & DEVELOPMENT CO. LTD. et al.			

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 9 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
 - a. ☐ sent to the applicant and to the International Bureau a total of sheets, as follows:
 - ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand 29.05.2005	Date of completion of this report 21.11.2005
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Nichogiannopoulou, A Telephone No. +49 89 2399-8054 

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/IL2004/001018

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-48 as originally filed

Claims, Numbers

1-40 as originally filed

Drawings, Sheets

1/8-8/8 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/IL2004/001018

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1-40 all partially and 7, 29-36 and 39 with regard to industrial applicability

because:

- ☒ the said international application, or the said claims Nos. 7, 29-36 and 39 with regard to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for the said claims Nos. 1-40 all partially

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

- ☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IL2004/001018

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-16, 26-36, 38-40
	No: Claims	17-25, 37
Inventive step (IS)	Yes: Claims	1-16, 26-36, 38-40
	No: Claims	17-25, 37
Industrial applicability (IA)	Yes: Claims	1-6, 8-28, 37, 38, 40
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/IL2004/001018

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☐ received by this Authority as an amendment on
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/IL2004/001018

Re Item I

Basis of the report

1. The basis of this report is the application as originally filed.

Re Item II

Priority

1. The following document was published prior to the international filing date but later than the priority date claimed (P-document):

P1: KAHN JOY ET AL: "Overexpression of CXCR4 on human CD34+ progenitors increases their proliferation, migration, and NOD/SCID repopulation" BLOOD, vol. 103, no. 8, 15 April 2004 (2004-04-15), pages 2942-2949, XP002324814
ISSN: 0006-4971

2. The priority document pertaining to the present application was not available at the time of establishing this first written opinion. Hence, the current assessment is based on the assumption that all claims enjoy priority rights from the filing date of the priority document (13.11.2003). If it later turns out that this assumption is incorrect, **P1** will become relevant to the assessment of whether the present application satisfies the criteria set forth in Article 33(2) and (3) PCT.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. No meaningful examination could be performed for claims 1-40 all partially and 7, 29-36 and 39 with regard to industrial applicability, for the following reasons:
 - 1.1. Rule 66. 1.(e) (PCT):
No complete international search report has been established for claims 1-40 all partially (see Form PCT/ISA/210). Accordingly, said claims will be the subject of international preliminary examination, in as far as they cover human haematopoietic

stem cells only.

2. Claims 7, 29-36 and 39 -as far as they concern *in vivo* methods- relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with regard to industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

- D1: SAWADA S ET AL: "DISTURBED CD4+ T CELL HOMEOSTASIS AND IN VITRO HIV-1 SUSCEPTIBILITY IN TRANSGENIC MICE EXPRESSING T CELL LINE-TROPIC HIV-1 RECEPTORS" JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP, vol. 187, no. 9, 4 May 1998 (1998-05-04), pages 1439-1449, XP000866065 ISSN: 0022-1007
- D2: LOUACHE FAWZIA ET AL: "Expression of CD4 by human haematopoietic progenitors" BLOOD, vol. 84, no. 10, 1994, pages 3344-3355, XP002324832
- D3: KOLLET ORIT ET AL: "Human CD34+CXCR4- sorted cells harbor intracellular CXCR4, which can be functionally expressed and provide NOD/SCID repopulation" BLOOD, vol. 100, no. 8, 15 October 2002 (2002-10-15), pages 2778-2786, XP002324815 ISSN: 0006-4971

2. **Novelty and Inventive step** (Article 33(2) and (3) PCT)
 - 2.1. The present application discloses that over-expression of recombinant CXCR4 (the SDF-1 receptor) on CD34⁺ haematopoietic stem cells (HSCs) from human cord blood and mobilized peripheral blood, results in preservation and/or expansion of the CD34⁺/CD38⁻ primitive population and in enhanced sensitivity to low concentrations of SDF-1. It could also be shown that overexpression of CXCR4 partially prevents

deterioration or cleavage of the 6H8 epitope, shown to play a role in the CXCR4 chemotactic function.

2.2. **D1** discloses transgenic mice expressing CXCR4 on their CD4⁺ cells.

D2 discloses that human haematopoietic stem cells express low levels of the T cell antigenic determinant CD4.

D3 discloses that enhancement of endogenous CXCR4 expression on human CD34⁺ HSC upon culture with cytokines, enhances their homing ability in immunodeficient mouse bone marrow.

2.3. The available prior art does not disclose or suggest the recombinant overexpression of CXCR4 on haematopoietic stem cells. The subject matter of claims 1-16, 26-36, 38-40 is thus novel and inventive under the terms of Articles 33(3) and (4) PCT.

2.4. Product claims 17-25, 37 however, are defined by the process they are obtainable by. It is hereby noted that for a product to be considered novel, the product has to be novel *per se*, irrespective of the method it is obtainable by. In light of **D1** and **D2** it becomes evident that said claims cannot possibly be considered novel or inventive under the terms of Article 33(2) and (3) PCT.

3. **Industrial applicability** (Article 33(4) PCT)

The subject-matter of the claims for which an opinion has been established (see item III) appears to be industrially applicable under the terms of Article 33(4) PCT.

Re Item VIII

Certain observations on the international application

1. Present claims 1-3, and 17 do not satisfy the provisions of Article 6 PCT in that the

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/IL2004/001018

terms "high", "improved", and "low" used therein are unclear. These terms are merely relative terms that do not attribute any directly and unambiguously recognisable technical features to the entities they relate to.